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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,306	12/13/2001	Kevin P. Baker	GNE.2830P1C66	7268

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/017,306	**Applicant(s)** BAKER ET AL.	
	Examiner Bridget E. Bunner	**Art Unit** 1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *08 September 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *32,33,38 and 44-47*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 5. Applicant's reply has overcome the following rejection(s): The objection to claim 38 is withdrawn in view of the amendment to claim 38 in the response of 03 June 2005.

Continuation of 11. does NOT place the application in condition for allowance because:

Claims 32-33, 38, and 44-47 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Applicant's arguments (03 June 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that one of skill in the art would readily understand that a protein which inhibits glucose uptake into adipocytes is a potential therapeutic target, since blocking the function of this protein would decrease the inhibition, and thus increase glucose uptake into adipocytes. Applicant argues that one of skill in the art would further understand that antagonists to the PRO1760 polypeptide include antisense oligonucleotides, such as those which may be derived from the claimed polynucleotides. Applicant indicates that the claimed polynucleotides are useful in the therapeutic treatment of disorders wherein stimulation of glucose uptake by adipocytes is expected to be therapeutically effective, such as obesity, diabetes, and hyper- or hypo-insulinemia. Applicant's arguments have been fully considered but are not found to be persuasive. The proposed use of the PRO1760 polypeptides and the claimed PRO1760 polynucleotides as potential therapeutic targets is simply a starting point for further research and investigation into potential practical uses of the polypeptides and polynucleotides.

Applicant also contends that Mueller et al. (1998) disclose that inhibitors of adipocyte glucose uptake inhibit leptin gene expression and leptin secretion from adipocytes. Applicant argues that one of skill in the art would have understood that agents capable of modulating leptin regulation would be useful in investigations regarding the treatment of obesity. Applicant states that PRO1760, as an inhibitor, would be useful as a pharmacological tool for invesigation of leptin regulation. Applicant's arguments have been fully considered but are not found to be persuasive. The specification of the instant application does not teach that PRO1760 is involved in leptin regulation. Furthermore, the proposed use of the claimed PRO1760 polypeptides and polynucleotides as potential therapeutic tools to investigate leptin regulation is simply a starting point for further research and investigation into potential practical uses of the polypeptides and polynucleotides.

The polynucleotide, polypeptide, and antibody do not have a substantial utility because basic research is required to study the properties and activity of the polynucleotide that encodes the polypeptide of SEQ ID NO: 376. Until some actual and specific significance can be attributed to the protein identified in the specification as PRO1760, the instant invention is incomplete. In the absence of knowledge of the biological significance of this protein, there is no immediately obvious patentable use for it. Since the instant specification does not disclose a "real world" use for PRO1760 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claims 32-33, 38, and 44-47 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. However, even if the claimed invention is eventually deemed to have a credible, specific and substantial asserted utility or a well established utility, claims 32 and 44-47 would remain rejected under 35 U.S.C. § 112, first paragraph.

Applicant states that a specific and substantial asserted utility has been disclosed, as described above. Applicant also argues that once a one of skill in the art could identify whether the variant SEQ ID NO: 375 sequence falls within the parameters of the invention. Applicant argues that one of skill in the art could readily test a polypeptide encoded by the variant nucleic acid sequence to determine whether it inhibits the uptake of glucose or FFA by adipocyte cells by the methods set forth in the specification. Applicant states that the claims recite polypeptide sequences associated with a biological activity and that this biological activity together with the well defined high degree of sequence identity and knowledge in the art defines the claimed genus such that one of skill in the art would have known how to make and use the claimed polypeptide sequences without undue experimentation. Specifically, since Applicant has not provided evidence to demonstrate that the PRO1760 polynucleotide and polypeptide have a specific and substantial asserted utility or a well established utility,

one skilled in the art would not know how to use the claimed invention. Furthermore, the broad brush discussion of making and screening for allelic variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the PRO1760 polypeptide of SEQ ID NO: 376 and polynucleotide of SEQ ID NO: 375 are disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such trial and error experimentation is considered undue. Certain positions in the polypeptide sequence are critical to the protein's structure/function relationship, e.g., such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions). Additionally, recitation of the phrase "the nucleic acid encodes a polypeptide that inhibits the uptake of glucose or FFA by adipocyte cells" in the claims is not adequate to describe nucleic acid variants that have at least 99% homology to the PRO1760 nucleic acid, since there was no reduction to practice to support the claims. Proper analysis of the Wands factors was provided in the previous Office Action.

Claims 32 and 44-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant asserts the genus of polynucleotides with at least 99% sequence identity to SEQ ID NO: 375, wherein the nucleic acid encodes a polypeptide which possess the functional property of inhibiting the uptake of glucose or FFA by adipocyte cells would meet the requirement of 35 U.S.C. § 112, first paragraph, as providing written description. Applicant argues that the specification provides detailed guidance as to changes that may be made to a PRO polypeptide without adversely affecting its activity. Applicant's arguments have been fully considered but are not found to be persuasive. Applicant has not described or shown possession of all polynucleotides 99% homologous to SEQ ID NO: 375, that still retain the function of SEQ ID NO: 375. Nor has Applicant described a representative number of species that have 99% homology to SEQ ID NO: 375, such that it is clear that they were in possession of a genus of polynucleotides functionally similar to SEQ ID NO: 375. Even one skilled in the art could not envision the detailed chemical structure of all or a significant number of encompassed PRO1760 polynucleotides, and therefore, would not know how to make or use them.
The broad brush discussion of making and screening for variants in the instant specification does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the PRO1760 polynucleotide of SEQ ID NO: 375 is disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants. The fact pattern in the instant application is not analogous to Example 14 in the Revised Interim Written Description Guidelines. In Example 14 of the Guidelines, the protein and variants have a specific activity disclosed in the specification. However, regarding the PRO1760 polynucleotides and polypeptides of the instant invention, the specification does not teach any significance of the PRO1760 polynucleotide or polypeptide. Recitation of the phrase "the nucleic acid encodes a polypeptide that inhibits the uptake of glucose or FFA by adipocyte cells" in the claims is not adequate to describe the PRO1760 nucleic acid variants that have at least 99% homology to the PRO1760 nucleic acid, since there was no reduction to practice to support the claims.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER